REMARKS

A. Status of the Claims

Claims 1, 13-15, and 17 have been amended to correct typographic errors. No new matter is added. Claims 1, 4-6, 8-10, 13-18, 21-23, 25-27, 30-33, and 38-39 are currently pending and presented for reconsideration.

B. Claim Objection

The Official Action objects to claim 1 for a misspelling of the term "geneticin". As noted above, claim 1 has been amended to correct this typographic error, and Applicants respectfully submit that the objection is now moot.

C. Claim Rejection Under 35 U.S.C. § 112, First Paragraph- Enablement

The Action rejects claims 1, 4-6, 8-10, 13-18, 21-23, 25-27, 30-33, and 38-39 under 35 U.S.C. 112, first paragraph, because the Specification is asserted to not reasonably provide enablement for a method of detecting the presence of any selectable marker gene in a plant using all the listed selective agents and organosilicone concentrations.

In response, Applicants traverse, and note that the claims do not relate to a method for detecting the presence of "any" selectable marker gene by applying "any" amount of "any" selective agent, but rather to a method for detecting the presence of a selectable marker gene product that corresponds with one or more of the listed selective agents (*e.g.* kanamycin, paromomycin, ribostamycin, butirosin, and geneticin; see claims 1 and 17), all of which are related aminoglycoside antibiotics as is well known in the art. Further, specific selective agents are explicitly listed in claims 1 and 17, and an "effective amount" of selective agent is specified in claim 17, while the working examples provide clear examples of application ranges for both selective agents and organosilicone surfactants, as well as discussions of the symptoms induced

on transgenic and non-transgenic plants following application of these various concentrations of selective agents and surfactants. For instance, see Examples 1 and 3 for guidance relating to concentrations of surfactant to be used; Examples 2 and 4 for guidance on use of appropriate quantities and volumes of selective agents; Examples 5-8 for guidance on use of kanamycin, paromomycin, and mixtures of the two selective agents; Example 9 for use of alternative surfactants; Example 10 regarding application to soybean plants; and Example 11 for environmental conditions for plant growth. One of skill in the art, using the extensive guidance in the specification, could routinely determine appropriate experimental conditions with respect to these parameters.

The Action also asserts that direct application of a selectable marker and a surfactant to plants is unpredictable, noting for instance that use of SILWET L-77 at concentrations above 0.1% resulted in yellowing of leaves that would likely interfere with ability to score plants for the presence of a selectable marker gene product (Example 1). Applicants traverse, noting that this data mentioned in Example 1 is clearly from a preliminary experiment that does not even include application of a selective agent. Instead, this information was used to guide subsequent studies (*e.g.* Examples 2-8), that result in a highly predictable method for determining the presence of a selective marker gene product.

Thus, Example 6 (page 17, lines 16-18) states that ELISA protein results for the presence of a linked Bt transgene correlated with the selectable marker gene product results in 296/297 corn plants, a rate of 99.66%, while Example 10 shows development of assay conditions allowing for determination of the presence of the NptII gene product in soybean plants, for instance in the presence of 0.06% SILWET L-77 and 5000 mg/L kanamycin and paromomycin (Specification, page 20, lines 7-8). Clearly, conditions are demonstrated wherein 100% of

treated non-transgenic soybean plants showed necrosis in the presence of the selective agent and SILWET L-77, while 0% of transgenic soybean plants showed such necrosis, a highly predictable outcome. One of skill in the art would clearly understand that the precise level of selective agent and surfactant to be applied could vary with the plant species, the transgene construct thought to be present, and the age or growth conditions of the plant, but determining effective levels would require only routine experimentation in view of the guidance provided.

The Action also asserts that use of different organosilicone surfactants is unpredictable. Applicants traverse, and note that Example 9 clearly demonstrates that numerous organosilicone surfactants provided similar results to SILWET L-77. Although the Action singles out one surfactant, SILWET L-7002, to point out that one plant out of 6 that failed to display an expected symptom and showed no visible bleaching, Applicants respectfully submit that this one plant was the only one, out of 42 tested (6 plants for each of 7 compared surfactants) that gave such a false positive result. Fully 97.6% of the tested plants gave phenotypes as expected. One of skill in the art would clearly understand that the use of alternative surfactants is thus demonstrated to be highly predictable as compared to SILWET L-77. The working examples provide explicit guidance for selecting appropriate ranges of concentrations of selective agents and for surfactants, thus clearly demonstrating various conditions under which the presence of a selectable marker gene may be detected, and the extensive use of control treatments and ranges of application for the selective agents and surfactants provides clear guidance for determining effective levels of each under the various described growth conditions. This guidance may be routinely used by one of skill in the art if other conditions are desired.

The Action asserts, at page 5, that a reference by Deckeyser (1989) alleges that use of certain selection agents can be "very concentration dependent", and Zhou *et al.,* 1995 is alleged

to state: "few selectable markers are currently available for genetic transformation of monocot species". Applicants note that these references were published at least several years prior to the date of the present application, and thus are not shown to represent the state of the art at the filing date. Indeed, the specification discloses that numerous selective agents were known for transformation of plants, including monocots, as of the priority date for the present application (*e.g.* Specification, page 5, lines 2-5), and Kanamycin and other aminoglycosides were routinely used in the art to select transformed plant cells (*e.g.* see Cornelissen *et al.,* WO 1994/026913, published November 24, 1994). However, regardless, experimentation to determine the proper concentration of selective agent for a given experiment would be routine in view of the specification's teachings, and not undue, as noted below.

The Action further asserts at page 4 that the claims encompass all or many herbicide and antibiotic selectable agents and corresponding resistance genes, and that three antibiotics corresponding to a single resistance gene behave unpredictably in the described assays. Applicants respectfully traverse, noting that claims 1 and 17 recite a defined group of selective agents, and thus the corresponding selectable marker genes and gene products are correspondingly limited. Additionally, as geneticin did not confer phytotoxic symptoms on the tested plants, no conclusion can be drawn regarding its use in conjunction with use of organosilicone surfactants in the presently claimed method. However, Applicants submit that, as noted in the Action at page 5, and below in the Response, geneticin is a well known selective agent for plant cell culture, for instance in the reference of Hauptmann *et al.* cited by the Action. Applicants also submit that use of geneticin in the presently claimed method would require no more than routine experimentation to determine, whether for corn, soybean, or another plant,

what would be appropriate selective conditions so that it may be used in conjunction with an organosilicone surfactant in the method of the present invention.

Regarding kanamycin and paromomycin, as noted above, the data at page 16 indicates that paromomycin was highly effective in allowing determination of the presence of a selectable marker gene product, especially in combination with kanamycin, and as compared with the control treatments performed in the absence of surfactant. In other words, the present claims do not relate simply to the efficacy of the use of paromomycin or other selective agent for selection of transgenic plants. Rather, they relate to a method that utilizes an organosilicone surfactant to enhance the ability to detect the presence of a selectable marker gene product in a putatively transgenic plant. Thus, the use of organosilicone surfactants in the presently claimed methods is not rendered unpredictable simply because a given selective agent occasionally yields inconclusive selection phenotypes under a certain set of conditions. The presence of inoperative embodiments (if that is indeed what they are) within the scope of a claim does not necessarily render a claim nonenabled (MPEP 2164.08(b), since identifying appropriate selective conditions for any given putatively transformed plant would be routine, and not undue.

The Action further states that the amount of antibiotic and organosilicone surfactant needed as a function of the age of the plants would be unpredictable, providing Example 4 to demonstrate this. However, Applicants respectfully submit that, in view of the detailed guidance in the Specification, such experimentation to determine useful conditions regarding plant age, and the amount of antibiotic and surfactant needed would not be undue, but would be routine. One of skill in the art would clearly understand the need to routinely determine appropriate conditions with regard to age of plant, growth conditions, amount of selective agent needed,

amount of surfactant needed, and to include appropriate controls, just as is done in Examples 1-11.

The Action also asserts that not all markers that work in the selection of transformed dicots also work for monocots or other given plant species. Applicants respectfully submit that determining the precise conditions for use of a selective agent on plant cells and plants is not within the scope of the present claims which relate to use of an organosilicone surfactant to determine the presence of a selectable marker gene product. Further, the experimentation alleged to be needed would be routine, and would be carried out in the context of obtaining the putatively transformed plants in the first place, that is separately from the presently claimed method. Thus Applicants respectfully submit that this argument has no bearing on the enablement of the present claims.

The Action also asserts that undue experimentation would be required to identify and use selection agents in addition to kanamycin and paromomycin. Applicants again traverse, noting that the Action itself, at page 5, notes that various selection agents may be useful, each under a given set of conditions. Thus, the Action states that geneticin is in fact a useful selection agent for *Lolium* as reported by Hauptmann *et al.* This clearly shows that undue experimentation would not be necessary to identify appropriate conditions for practicing the invention for instance from a routine scientific literature search. And, again, Applicants note that the presently claimed method does not relate to the efficacy of any given agent for selection of plants, but to the use of an organosilicone surfactant in a method to determine the presence of a selectable marker gene product. The Specification clearly demonstrates conditions under which distantly related plants (*e.g.* corn and soybeans) may be utilized in practicing the invention (*e.g.* Examples 5,6, and 10 among others), and one of skill in the art would be aware that, for instance, the NptII

marker gene product has been among the most widely used selectable markers for creating transgenic plants, and may be used in conjunction with any of several related aminoglycoside antibiotics to effect plant cell selection.

D. Claim rejection under 35 U.S.C. § 101 – Double Patenting

Applicants note that their statement regarding the filing of a terminal disclaimer, if needed, is acknowledged (page 7), and respectfully request that the rejection be removed in view of this.

E. Conclusion

In view of the above, it is submitted that the rejections to the claims have been overcome, and the case is in condition for allowance.

The Examiner is invited to contact the undersigned attorney at (512) 536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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